

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1-23 (cancelled)

24 (currently amended). A method of reducing the level and/or activity of a target protein in an eukaryotic cell via the activation of ubiquitination of said target protein comprising contacting said cell with a compound comprising;

- a) a ubiquitination recognition element which is able to bind to either the E3 or E2 elements of a ubiquitination system, wherein said ubiquitination recognition element has a molecular weight less than 30,000 and has a binding affinity for said E3 and/or E2 elements of the ubiquitination system of at least 10^4 M^{-1} and;
- b) a target protein binding element that is able to bind specifically to said target protein wherein said target protein binding element has a molecular weight of less than 30,000 and has a binding affinity for said target protein greater than 10^5 M^{-1} ,

wherein said ubiquitination recognition element is covalently linked to said target protein binding element, and wherein the level and/or activity of the target protein in the eukaryotic cell is reduced.

25 (previously presented). The method of claim 24 where said reduction causes a physiological or metabolic change.

26 (previously presented). The method of claim 24 where said reduction causes a pharmacological change.

27 (previously presented). The method of claim 24 where said reduction treats a disease.

28 (original). The method of claim 24 where said contacting said cell is achieved by administering said compound to a mammal.

29 (previously presented). The method of claim 28 where said target protein is an antigen.

30 (original). A method as in claim 29 wherein said mammal is a human.

31-35 (cancelled).

36 (previously presented). A method of selectively targeting ubiquitination in a cell comprising contacting said cell with a compound comprising;

a ubiquitination recognition element which is able to bind to either the E3 or E2 functional elements of a ubiquitination system, wherein said ubiquitination recognition element has a molecular weight less than 30,000 and has a binding affinity for said E3 and/or E2 elements of the ubiquitination system of at least 10^4 M^{-1} and;

a target protein binding element that is able to bind specifically to a target protein wherein said target protein binding element has a molecular weight of less than 30,000 and has a binding affinity for said target protein greater than 10^5 M^{-1} ,

wherein said ubiquitination recognition element is covalently linked to said target protein binding element.

37 (original). The method of claim 36 where said ubiquitination recognition element is recognized by an E3 for the N-end rule.

38-39 (cancelled).

40 (original). A method as in claim 24 wherein said compound activates the ubiquitination of a protein bound to said target protein.

41-42 (cancelled).

43 (previously presented). The method of claim 24 wherein said ubiquitination recognition element has a molecular weight between 50 and 10,000.

44 (new). A method for reducing the level and/or activity of a target protein comprising:

i) contacting the target protein with a compound comprising;

a) a ubiquitination recognition element which is able to bind to either the E3 or E2 elements of a ubiquitination system, wherein said ubiquitination recognition element has a molecular weight less than 30,000 and has a binding affinity for said E3 and/or E2 elements of the ubiquitination system of at least 10^4 M^{-1} and;

b) a target protein binding element that is able to bind specifically to a target protein wherein said target protein binding element has a molecular weight of less than 30,000 and has a binding affinity for said target protein greater than 10^5 M^{-1} ,

wherein said ubiquitination recognition element is covalently linked to said target protein binding element, and wherein the level and/or activity of the target protein is reduced.

45 (new). The method as in claim 44 and further comprising:

- i) exposing said target protein to said ubiquitination system and;
- ii) exposing said target protein to a ubiquitin-dependent proteolytic system.

46 (new). The method as in claim 44, wherein said ubiquitination recognition element has a molecular weight between 50 and 3,000.

47 (new). The method as in claim 44, wherein said target protein binding element has a molecular weight less than 5,000.

48 (new). The method as in claim 47, wherein said ubiquitination recognition element has a binding affinity greater than 10^4 M^{-1} .

49 (new). The method as in claim 48, wherein said target protein binding element has ClogP less than 6.

50 (new). The method as in claim 49, wherein said target protein binding element has less than 50 H-bond donors.

51 (new). The method as in claim 50, wherein said target protein binding element has a sum of N and O atoms less than 100.

52 (new). The method as in claim 44, wherein said compound further comprises an intracellular delivery element.

53 (new). The method as in claim 52, wherein said intracellular delivery element comprises a peptide.

54 (new). The method as in claim 53, wherein said peptide is selected from the group consisting of transportan, homeobox peptides, antennapedia residues 43-58, invasion and galparan.

55 (new). The method as in claim 44, wherein said ubiquitination recognition element and said target protein binding element are not peptides.

56 (new). The method as in claim 44, where in said ubiquitination recognition element has a molecular weight less than 5,000 and said target protein binding element has:

- a ClogP of less than 6;
- less than 50H-bond donors;
- the sum of N and O atoms less than 100.